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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,324	12/10/2001	Francis J. Martin	55325-8148.US06	4133

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EXAMINER
KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/016,324	Martin
Examiner	**Art Unit**
Gollamudi Kishore	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-59* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The preliminary amendments dated 12-10-01 are acknowledged.

Claims included in the prosecution are 29-59.

Claim Rejections - 35 USC § 112

1.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 30-33, 37-39 and 58-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There should be a comma between distearoylphosphatidylcholine and sphingomyelin in claim 30.

It is unclear what applicants intend to convey by 'shielded cationic lipid to impart a positive liposome-surface charge. Shielded by what?

'the hydrophilic polymers' in claim 37 lacks an antecedent basis in claim 29.

The liposomes in claim 29 have already a coating of a hydrophilic polymer. The location of the diblock polymer as recited in claim 58 in relation to said hydrophilic polymer in claim 29 is unclear. Clarification is requested.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless -**
>
> **(e) the invention was described in-**
> **(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or**
> **(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).**

4. Claims 29-31, 33-37, 39 and 40-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Marshall (5,939,401).

Marshall discloses liposome formulations containing a cationic amphiphile, DOPE and PEG (5000)-DMPE for the administration of therapeutic molecules by inhalation. The biological molecules include proteins, small molecules, RNA and DNA. The cationic lipids include cholesterol carbamate derivatives (note the abstract, col. 34, line 27 et seq., col. 54, line 31 et. Seq.).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. **Claims 29-30, 34-37, 39-41, 44-49 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 86/06959 in combination with Klibanov (J. Liposome Research, 1992) both are of record.**

WO 86 teaches liposomal formulations and a method of administering the formulations by inhalation. The liposomes are made from a variety of phospholipid combinations and having sizes of less than 5 microns. The encapsulated drugs include interferon (note the abstract, pages 8, 11, 12, 14, 19, 27, 28 and Examples). What is lacking in WO 86 is the teaching of the coating of the liposomal surface with a hydrophilic polymer.

Klibanov teaches that when the liposomal surface is coated with a hydrophilic layer of oligosaccharides, glycoproteins, polysaccharides and synthetic polymers such as PEG, the liposomes avoid the RES and circulate in blood for longer periods. Klibanov further teaches the targeting the liposomes using ligands such as biotin, proteins and antibodies (note the entire publication).

The coat the liposomes of WO 86 with a hydrophilic polymer would have been obvious to one of ordinary skill in the art because such a coating would enable the liposomes to circulate longer and reach the target tissue as taught by Klibanov.

7. Claims 29-31, 33-37, 39 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marshall cited above by itself or in combination with WO 86/06959 cited above.

As pointed out above, Marshall discloses liposome formulations containing a cationic amphiphile, DOPE and PEG (5000)-DMPE for the administration of therapeutic molecules by inhalation. The biological molecules include proteins, small molecules, RNA and DNA. The cationic lipids include cholesterol carbamate derivatives (note the abstract, col. 34, line 27 et seq., col. 54, line 31 et. Seq.). Marshall does not provide a specific example showing the administration by inhalation. It would have been obvious to one of ordinary skill in the art to use this mode of administration of liposomes suggested by Marshall since the mode of administration is the choice of the practitioner. One of ordinary skill in the art would be motivated to use the inhalation route since WO shows the this route as a successful mode of administration of liposomes.

8. Claims 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marshall cited above by itself or in combination with WO 86/06959 cited above, further in view of Gao (BBRC, 1991).

Marshall teaches cholesterol derivatives, but not instantly claimed dimethylaminoethane carbamoyl cholesterol.

Gao teaches that instant carbamoyl cholesterol in liposomes is very effective transfecting agent (note the abstract). It would have been obvious to one of ordinary skill

in the art to use instant carbamyl cholesterol derivative in Marshall's liposomes since Gao teaches that this cationic lipid is an effective transfection agent.

9. Claims 49-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 86/06959 in combination with Klibanov (J. Liposome Research, 1992) both are of record, further in view of Chestnut (5,800,815), DeFrees (5,604,207) and applicant's statements of prior art.

The teachings of WO and Klibanov have been discussed above. Neither WO nor Klibanov teach instantly claimed antibodies and ligands.

Chestnut teaches targeting of liposomes using selectin antibodies (note col. 21).

DeFrees teaches targeting of liposomes using sialyl Le (note columns 47 and 48).

Applicants indicate that the claimed antibodies and other ligands are art known (see Table I on page 23).

It would have been obvious to one of ordinary skill in the art to use art known ligands in the teachings of WO and Klibanov since Klibanov teaches that targeting ligands such as proteins and antibodies can be attached to the liposomal surface and the references of Chestnut and DeFrees further provide guidance as to use of the ligands such as selectin antibodies and sialyl Le along with liposomes.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

September 5, 2002